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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/829,073	04/09/2001	Ke-Wen Dong	#651	7413

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/829,073	DONG ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *10-18,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response under 37 CFR 1.111

1. Applicant's response to the Office Action mailed 20 April 2004 is acknowledged (filed July 20, 2004).

Response to Arguments

2. Applicants contend that the prior art rejections under 35 USC 103 (a) would not have suggested one of ordinary skill in the art to make the proposed modification and there was not reasonable expectation of success. Specifically, Applicant argues that Whitmarsh et al. did not teach the importance of glycosylated rhZP3 and its function in sperm binding and the acrosome reaction. While, neither Whitmarsh et al. nor Chamberlin/Dean taught the expression of rhZP3 from a human ovarian cell (oocyte). This argument was carefully considered and found persuasive. Accordingly, the rejections under 35 USC 103(a) have been modified to include the reference to Chapman and Barratt.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitmarsh et al. (Molecular human Reproduction, Vol.2, No.12, pages 911-919) in view of Chapman and Barratt (Molecular Human Reproduction, Vol.2, No.10, pages 767-774, 1996) and further in view of Franken et al. (Fertility and Sterility, Vol.66, No.6, December 1996).

Whitmarsh et al. disclose a method for measuring the biological activity of recombinant human ZP3 (rhZP3). In the method rhZP3 is immobilized on beads and exposed to spermatozoa.

The binding between the rhZP3 and sperm is accessed sperm function/activity and the acrosomal status. See abstract, page 914, and page 915. Whitmarsh et al. do not specifically teach that the rhZP3 is glycosylated but does give the means by which the rhZP3 can be glycosylated [incorporation of canine pancreatic microsomal membranes] and detected [Amersham Ltd]. See Page 916 1st column, 2nd paragraph. Whitmarsh et al. also teach the increased binding seen in glycosylated constructs versus the non-glycosylated molecules. The researchers state, "In the present study the rhuZP3 was probably not glycosylated, yet retained some biological activity. This is perhaps surprising if we confine our thoughts to the mouse where conventional wisdom emphasizes the importance of carbohydrates [glycosylation]in the binding of spermatozoa to the zona." See page 917 1st column – 2nd paragraph. Accordingly gylcosylated forms and non-glycosylated forms of rhZP3 were known and taught in the prior art.

Whitmarsh et al. also teach that although their results exhibited increased binding of rhuZP3 coated beads when compared with controls, the overall (median) binding of rhZP3 was low – only 20%. Page 916, 2nd column 2nd paragraph, lines 15-17.

Whitmarsh et al. differ from the instant invention in not specifically teaching the importance of glycosylation of rhZP3 in sperm binding.

However, Chapman and Barratt disclose this limitation. Chapman and Barratt teach the importance of ZP3 glycosylation in sperm binding. The reference also teaches the importance of ZP3 glycosylation in mammalian fertilization. In particular, the sperm-binding capacity of mouse ZP3 resided within the O-glycosylation present on the ZP3 glycoprotein. Removal of O-linked carbohydrates prevented sperm-zona interaction and the removal of N-linked carbohydrates negligibly effected sperm binding activity. See page 768, 1st column 2nd paragraph – Glycosylation and Fertilization. In their findings rhZP3 was immobilized on agarose beads, which bound sperm and induced the acrosome reaction. Page 772, 2nd column last 6 lines.

It would have been obvious to one of ordinary skill in the art to utilize a glycosylated rhZP3 as taught by Chapman and Barratt in the method of Whitmarsh et al. in order to increase sperm binding. Whitmarsh et al. taught low overall binding –only 20% with their recombinant non-glycosylated human ZP3 (Page 916, 2nd column 2nd paragraph, lines 15-17) while Champman and Barratt taught that the binding affinity between the spermatozoon and zona (ZP3) is dependent on glycosylation. See page 768, 1st column, 4th paragraph and Introduction on page 767. Therefore to study sperm – ZP3 binding one of ordinary skill in the art would have employed glycosylated ZP3 because the prior art taught the importance of glycoslyation in this binding activity.

One of ordinary skill would have been motivated to employ a glycosylated rhZP3 to increase binding or fertility.

Whitmarsh et al. in view of Chapman and Barratt differ from the instant invention in not specifically rhZP3 expressed from human ovarian cells.

In this regard, Franken et al. teach the expression of human ZP from oocytes derived from postmortem ovarian material. See abstract and page 1010 (Collection and Solubilization of ZP).

With respect to the recombinant human ZP3 being expressed by human In other words the true binding between sperm and the zona (ZP3) is assessed when the two components are from the same species. One of ordinary skill would have been motivated to use a human ZP3 expressed from human ovary cells to bind human sperm in order to acquire accurate data with respect to human binding events.

II. Claims 2-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitmarsh et al. (Molecular human Reproduction, Vol.2, No.12, pages 911-919) in view of Chapman and Barratt (Molecular Human Reproduction, Vol.2, No.10, pages 767-774, 1996) and further in view of Franken et al. (Fertility and Sterility, Vol.66, No.6, December 1996).

Please see previous discussions of Whitmarsh et al. in view of Chapman and Barratt and further in view of Franken et al. as set forth above.

Whitmarsh et al. in view of Chapman and Barratt and further in view of Franken et al. differ from the instant invention in not specifically identifying the concentration of human zona pellucida protein ZP3.

However, Whitmarsh et al. in view of Chapman and Barratt and further in view of Franken et al. disclose the claimed invention except for specific concentrations of ZP3. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the concentration of reagents to the specific concentrations in claims 2-8 in a binding assay as a means of optimizing the assay, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

III. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Whitmarsh et al. (Molecular human Reproduction, Vol.2, No.12, pages 911-919) in view of Chapman and Barratt (Molecular Human Reproduction, Vol.2, No.10, pages 767-774, 1996) and further in view of Franken et al. (Fertility and Sterility, Vol.66, No.6, December 1996) and Foster et al. (U.S.Patent#4,444,879).

The teachings of Whitmarsh et al. in view of Chapman and Barratt and further in view of Franken et al. are set forth above.

The cited references fail to teach the assay as a kit. However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a micro plate, positive controls, negative controls, standards, and instructions are taught. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the binding/detection assay as taught by Whitmarsh et al. in view of Chapman and Barratt and further in view of Franken et al. and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay.

Response to Arguments

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant contends that the reference to Whitmarsh et al. does not disclose the use of a properly glycosylated hZP3 produced in human cell lines in order to determine human sperm activity. This argument was carefully considered but not found persuasive because Whitmarsh et al. have been cited in combination with Chapman and Barratt (Molecular Human Reproduction, Vol.2, No.10, pages 767-774, 1996) and further in view of Franken et al. (Fertility and Sterility, Vol.66, No.6, December 1996). The references of Chapman and Barratt and further in view of Franken et al. teach the utility of a properly glycosylated hZP3. Please see Whitmarsh et al. wherein low overall binding –only 20% was seen with their recombinant non-glycosylated human ZP3 (Page 916, 2nd column 2nd paragraph, lines 15-17).

Also, Champman and Barratt taught that the binding affinity between the spermatozoon and zona (ZP3) is dependent on glycosylation. See page 768, 1st column, 4th paragraph and Introduction on page 767.

With respect to the Foster patent, Applicant argues that a diagnostic kit for sperm activity comprising a glycosylated recombinant human ZP3-expressed from a human ovarian cell is not disclosed. It is noted however that the reagents and methods for detecting sperm activity as recited in the claims are taught in the combination of Whitmarsh et al. in view of Chapman and Barratt and further in view of Franken et al. The Foster patent was cited to merely make obvious kit configurations. Accordingly the new rejections read on the instant claims.

4. For reasons aforementioned, no claims are allowed.

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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